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EXAMINER
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 11

Application Number: 09/603,320
Filing Date: June 26, 2000
Appellant(s): BURZYNSKI, STANISLAW R.

Matthew L. Madsen
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 1, 2002.

(1) Real Party in Interest

A statement identifying the real party in interest, Stanislaw R. Burzynski, is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. There are no related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the instant appeal.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct. No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 1-4, 8 and 19-23 stand or fall together as stated in the appellant's brief.

(9) Prior Art of Record

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

5,238,947 Hendry et al. 08-1993

Applicant's Admissions on page 3, lines 18-28.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-4, 8 and 19-23 are rejected under 35 U.S.C. 103. This rejection is set forth in prior Office Action, Paper Nos. 6 and 8.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 8 and 9-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over applicant's admissions regarding the prior art at pages 2-3 of the specification in view of Hendry et al (USPN 5,238,947), all of record in the previous office action.

Applicant discloses that compounds such as 3-phenylacetylamino-2,6-piperidinedione and its hydrolysis products are known to block a reaction in the pathway of cholesterol biosynthesis, and as a result these compounds may lower serum cholesterol level. See page 3, lines 18-28 in the specification particularly.

Applicant's admissions regarding the prior art do not expressly disclose any relationship between the sodium salt of phenylacetylglutamine and 3-phenylacetylamino-2,6,piperidinedione. Moreover, applicant's admissions do not expressly teach the therapeutic amounts employed

herein, nor do they teach compositions containing the elected compound, phenylacetylglutamine sodium.

Hendry et al. discloses that the initial hydrolysis product of 3-phenylacetylamino-2,6-piperidinedione is phenylacetylglutamine, which is produced in vivo from phenylacetic acid and glutamine. In fact, Hendry et al. teaches that 3-phenylacetylamino-2,6-piperidinedione may be cyclized from phenylacetylglutamine in vivo,(Col. 2 lines 40-44).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ phenylacetylglutamine (or any salt thereof) in lieu of 3-phenylacetylamino-2,6-piperidinedione as cholesterol lowering agents in methods to inhibit or treat hypercholesterolemia in an affected patient.

One of ordinary skill in the art would have been motivated to combine these teachings in order to employ phenylacetylglutamine sodium in a method of treating or inhibiting hypercholesterolemia because phenylacetylamino-2,6-piperidinedione is known to be hydrolyzed in a host in vivo to produce phenylacetylglutamine. Therefore, similar antihypercholesterolemic effects in the host (i.e. affected patient) for both compounds would be reasonably expected. Given the current state of the art, determining the active ingredient dosage level is well within the Skilled Artisan's purview and the benefits of achieving such maximization obvious, to said Skilled Artisan. The optimization of amounts of active ingredients to be employed is considered within the skill of the artisan.

Further, the incorporation of known active agents in compositions with pharmaceutical carrier materials is conventional in the art.

(11) Response to Argument

a. Lines 18-23 of page 3 of the specification is indeed an admission by the applicant and is thus correctly cited as prior art.

Applicant argues that the Examiner's position that page 3 of the specification, lines 18-23 constitutes an admission that it was known in the prior art that the recited compounds may lower cholesterol level is incorrect. In the section entitled **"Description of Related Art"** of the specification at page 3, lines 18-23, applicant admits:

"It has been known for some time that compounds such as 3-phenylacetylamino-2,6-piperidinedione and its hydrolysis products such as phenylacetic acid, and salts, precursors, and analogs thereof (together "3-phenylacetylamino-2,6-piperidinedione and its derivatives"), can block the formation of iso-pentenylpyrophosphate from 5-pyrophosphomevalonate, a reaction in the pathway of cholesterol biosynthesis; as a result these compounds may lower serum cholesterol levels."

Applicant relies on the grammatical structure of the passage as well as the sentences following the passage quoted herein immediately above to contend that the teachings of the passage were only known to the inventor. This argument is not persuasive for at least two reasons. First, this passage appears in a section of the specification entitled **"Description of Related Art"** which describes the background of the invention. Secondly, the phrase "It has been known for some time" implies that the novel and non-obvious aspects of the invention do not lie in the information contained in the clause immediately following the phrase. Given that applicant and/or his representative draft the specification, they are best able to disclose the novel and unobvious characteristics of the invention in the section entitled "Detailed Description of the Invention."

Applicant then distinguishes the instant case from *In re Nomiya*, 184 USPQ2d 607, stating that nowhere has applicant characterized the possibility that the compounds described in the claims could lower serum cholesterol levels as being part of "prior art." First, note that this passage appears in a section of the specification entitled **"Description of Related Art"** which describes the background of the invention. Secondly, note that the holding in *Nomiya* is broader than the applicant's characterization of it. *Nomiya* clearly states: "We see no reason why appellant's representations in their application should not be accepted at face value as admissions that Figs. 1 and 2 may be considered "prior art" for any purpose, including use as evidence of obviousness under section 103." *Id* at 612. Similarly, in the instant case applicant's admission appears in a section of the specification entitled **"Description of Related Art"** which describes the background of the invention. This admission is analogous to the labeling of the figures in *Nomiya* and could therefore be used as prior art in an obviousness rejection.

Applicant further argues that "a patent applicant's statement of the purpose of the work is not prior art." *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Note that the admission herein is distinguishable from Dow because it is not a "statement of purpose of the work" since it merely provides what "has been known for some time" in the art.

b. The obviousness rejection under 35 USC 103 over applicant's admissions regarding the prior art at pages 2-3 of the specification in view of Hendry et al (USPN 5,238,947) is proper since a prima facie case of obviousness has been established.

1.The Skilled artisan would have had both a motivation to combine the teachings of the prior art and a reasonable expectation of success.

Applicant argues that the combination of the alleged admission taken together with the teachings of Hendry et al. does not provide a reasonable expectation of success for the instantly claimed invention and that the cited prior art provides a "motivation to try". Applicant

argues that the mere fact that a compound in known to inhibit function of a single enzyme known to be involved in cholesterol biosynthetic pathway, cannot provide poof or reasonable expectation that using similar compounds would lower serum cholesterol. In support of this proposition applicant cites to a biochemistry text. Note that the biochemistry text merely teaches the possible causes (i.e., etiology) of hypercholesterolemia and not a method of reducing cholesterol. Moreover, applicant would have had a reasonable expectation of success since he has admitted at page 2-3 of the specification that 3-phenylacetylamino-2,6-piperidinedione and its derivatives are known to block a specific step in the cholesterol biosynthetic pathway, broadly. Hendry et al. teaches that the initial hydrolysis product of 3-phenylacetylamino-2,6-piperidinedione is phenylacetylglutamine, which is produced *in vivo* from phenylacetic acid and glutamine. Therefore, one of ordinary skill in the art would have had the motivation as well as a reasonable expectation of success to combine the prior art teachings in Hendry et al. with the prior art teachings discussed by applicant in the specification because 3-phenylacetylamino-2,6-piperidinedione and its derivatives known to block a specific step in the cholesterol biosynthetic pathway and in turn block cholesterol synthesis result in the lowering of blood cholesterol levels in vitro or in vivo broadly, as indicated by applicant's admissions regarding the prior art, or even merely in vitro as argued by applicant in Paper No. 7 would also block the same pathway and reduce blood cholesterol *in vivo* in a patient as well.

2. In the instant case, disclosure of in vitro activity renders the in vivo activity obvious.

Applicant's admissions do not address the presence or absence of a host, neither is there any mention of *in vitro* vs. *in vivo* application or employment of these compounds. Therefore, applicant's remarks regarding mere *in vitro* enzyme activity blockage in the prior art as

represented by his admissions in the specification are unpersuasive. Furthermore, even if, applicant's admissions in the specification regarding the prior art were limited to *in vitro* enzyme activity, it is well known in the pharmaceutical art that the purpose of *in vitro* experimentation with pharmaceutical actives is to ultimately administer the active composition *in vivo* to an affected host/patient for some sort of therapy. This sort of in vitro testing is conventional in the pharmaceutical art. In fact, applicant himself is cited in Hendry et al. to have used in vitro experimentation to predict therapeutic efficacy for later in vivo administration of the same pharmaceutical composition, see particularly col. 2, lines 16-48. This case is therefore distinguishable from the "obvious to try" line of cases because the compound is known to possess the desired activity *in vitro*. Consequently, one of ordinary skill in the art would have reasonably believed that 3-phenylacetylamino-2,6-piperidinedione and its derivatives known to block a specific step in the cholesterol biosynthetic pathway and in turn block cholesterol synthesis result in the lowering of blood cholesterol levels in vitro or in vivo broadly, as indicated by applicant's admissions regarding the prior art, or even merely in vitro as argued by applicant in Paper No. 7 would also block the same pathway and reduce blood cholesterol *in vivo* in a patient as well.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Mojdeh Bahar, J.D.
June 3, 2002

Conferees
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